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PCT

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(54) Title: NUTRITIONAL SUPPLEMENT (57) Abstract A nutritional supplement is prepared from <i>Macrocystis</i> algae meal, microcapsules of yeast, and powdered calcite from sea shells. The supplement improves the health and growth of dairy and beef cattle, horses, and chickens, and improves milk and egg production. Minerals and vitamins may be added to the supplement where desired to counteract metabolic deficiencies in the animal.		

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NUTRITIONAL SUPPLEMENT

BACKGROUND OF THE INVENTION1. Field of the Invention

5 This invention relates to nutritional supplements for livestock. More specifically, the invention relates to a combination of *Macrocystis* algae, yeast, calcite, and other minerals, and methods of supplementing animal feed to promote growth and productivity.

2. Related Art

10 Throughout history, people tending livestock have sought to provide a nutritious feed that provides good growth, health, and productivity of the animal. With ruminants such as cows, certain nutritional supplements are added to a feed blend to promote milk production, calving, and so on. Those raising horses try to optimize size and health by selecting a wholesome blend of food such as hay and oats and supplements. Poultry farmers use a feed blend that is intended to maximize the number, quality, and size of eggs, or to maximize growth.

15 U.S. patent no. 5,085,874 relates to a feed product comprising whey, dry yeast, and fat together with proteins, starch, and other components. U.S. patent no. 5,000,964 describes feedstuffs with low levels of yeast together with a carrier and other components. U.S. patent no. 5,211,980 discloses a lipid pellet having an algin component such as sodium alginate and other nutritive elements.

20 The prior art does not include a combination of natural components including *Macrocystis* algae, yeast, and calcite that is adjusted to the needs of a particular type of livestock, and provides excellent growth and performance.

SUMMARY OF THE INVENTION

A nutritional supplement according to the invention is prepared from algae, yeast, and a mineral component. The supplement acts as a metabolic corrector and improves the health and growth of dairy and beef cattle, horses, and chickens, and improves milk and egg production. Minerals and vitamins may be added to the supplement where desired to counteract metabolic deficiencies in the animal.

According to the invention, a nutritional supplement for animals contains *Macrocystis* algae meal, dry yeast, and a mineral component. Preferably, the algae is dried and crushed to a meal, the yeast is Ceba Sc in microcapsules, and the mineral component is powdered calcite from sea shells. In preferred formulations the *Macrocystis* algae comprises about 25-75% by weight, the yeast comprises about 10-50% by weight, and the powdered calcite comprises about 10-30% by weight. In an especially preferred formulation, the *Macrocystis* algae comprises about 50% by weight, the yeast comprises about 30% by weight, and the powdered calcite comprises about 20% by weight.

The invention also comprises a method of improving the health of an animal comprising combining crushed calcite with *Macrocystis* algae meal and microcapsulated yeast to provide a nutritional supplement, and feeding the supplement to the animal. The method may also comprise (a) measuring metabolite levels in a stable tissue of the animal; (b) identifying metabolites whose levels are lower than desired; (c) adding the identified metabolites to crushed calcite; (d) combining the calcite with *Macrocystis* algae meal and microcrystalline yeast to provide a nutritional supplement; and (e) feeding the supplement to the animal. The method preferably involves providing the supplement in an amount of about 0.1 g to 1.0 g per kg body weight.

The metabolic corrector has other beneficial applications. It can prevent and treat viral infections in animals, particularly poultry, when a therapeutically effective dose of a

combination of the metabolic corrector is administered orally. It can also promote physical and mental health in humans.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawing figures are provided to facilitate understanding the invention.

5 Fig. 1 illustrates milk production records for dairy cattle fed with the metabolic corrector as compared to controls.

Fig. 2 illustrates milk fat content for dairy cattle fed with the metabolic corrector compared to controls.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

10 In describing preferred embodiments of the present invention, specific terminology is employed for the sake of clarity. However, the invention is not intended to be limited to the specific terminology so selected, and it is to be understood that each specific element includes all technical equivalents which operate in a similar manner to accomplish a similar purpose.

In its preferred form, the metabolic corrector is prepared from three basic ingredients.
15 Other minerals and supplements may be added according to the specific needs of particular animals. The metabolic corrector is preferably made up as follows:

- 1) edible marine algae genus *Macrocystis*, crushed into a meal form - about 25-75% by weight, preferably about 50%;
- 2) yeast culture, preferably a live yeast such as Ceba Sc 47 in microcapsules - about
20 10-50% by weight, preferably about 30%; and
- 3) calcite, preferably from pulverized sea shells, as an excipient - about 10-30% by weight, preferably about 20%.

A preferred dosage is about 0.1 to about 1 gram per kg live weight of the animal in question, most preferably about 0.25 grams per kg. Other amounts, lower or higher, may be desirable
25 depending on the animals' particular needs.

In dry form, the metabolic corrector typically comprises about 85% dry matter and about 15% water. These proportions may vary depending on climate and storage conditions. It is typically fed dry, but may be added to warm water for consumption, in which case it forms a viscous, gelatinous preparation.

- 5 Mineral elements may be added to the calcite excipient as indicated in each case depending on the nutritional requirements of the animal. The calcite component generally contains substantial amounts of calcium, sodium, phosphorous, potassium, magnesium, and sulfur. Other minerals in the excipient may include cobalt, silver, boron, bromine, chromium, copper, iron, iodine, mangasene, molybdenum, nickel, strontium, vanadium, and zinc.
- 10 Typically, slow growing animal tissue such as poultry feathers, hair, hoof, or blood are sampled and analyzed by an assay for mineral content. The quantities of these elements are determined in each particular case by an analysis of blood, hair or feather samples. The qualitative and quantitative mineral content of the sampled tissues are compared to a standard source, such as the U.S. Department of Agriculture Minimum Daily Requirement Tables for the particular
- 15 species, referred to as Cantidad Suficiente Para 100, or quantity sufficient to reach 100% of the desired level, by weight or volume. If the level of a particular mineral in a test animal is below the recommended level, then an extra quantity of that mineral is added to the calcite excipient as a supplement to meet the animal's minimum requirements. The supplemental minerals are easily obtainable anywhere in the world without restriction.
- 20 Using the metabolic corrector in proportions adequate to each animal species in general optimizes the utilization of the available nutrients and coenzymes in the feed ration vital to normal metabolism. The metabolic corrector apparently acts as a nutritional "buffer," and allows for the adequate absorption of the metabolites in the feed ration, i.e., glucids, proteins (amino acids), vitamins, and macro and microelements.

The metabolic corrector of the invention has been found to have many beneficial effects with various animals. These benefits are described here in terms of numerical observations made during the course of recent experimental procedures.

Each animal species has different nutritional requirements that are carefully monitored
5 in the process of formulating the metabolic corrector. Minerals are added as necessary to the calcite excipient, to supplement the mineral content of animals whose levels fall below the currently updated USDA Minimum Daily Requirement Tables.

Dairy Cattle:

Ruminants more often than not present digestive disturbances as a result of man's
10 constant interference in their feed formulation. This exposes the milking cow to nutritional factors and conditions which tend to limit optimum milk production and often is the cause for toxic and semi-toxic levels of certain elements. When incorporated into the feed ration, the interaction of the metabolic corrector in the ruminal medium modifies the metabolism of the intestinal flora. This interaction increases the pH of the digestive medium to 6.9, a level which
15 is considered to be normal.

Cows under pasture feeding conditions tend to have a ruminal pH in the order of 5.9/6.2. This acid ruminal medium causes an alteration of the ruminal flora and therefore an alteration of the metabolic process with special emphasis on proteins. Approximately 80% of the protein in the ration is broken down in the rumen, and through the cellulitic (or cellular)
20 action of the flora, is converted into bacterial protein. The undigested protein is transformed into ammonia (hepatotoxic ammonia).

The high level of ammonia overtaxes the liver as ammonia is absorbed through the walls of the rumen in transit to the circulatory system. These conditions result in a loss of protein in the diet and predominant toxic state in the animal. The optimum ammonia concentration
25 content for an acceptable protein metabolism is in the order of 5 grams per every 100 milliliters

of ruminal fluid. Cows in the above examples have been found to have levels of 30 to 40 grams per 100 milliliters of ruminal fluid.

When the metabolic corrector is added to the daily ration, in an amount of about 100 grams per day for a cow of 1,100 lbs. live weight, after a period of time, the pH becomes
5 adjusted to a desirable level. Thereafter, bacteria and protozoans will function adequately in the breakdown of proteins thereby reducing the levels of ammonia and thus increasing bacterial protein.

From the actions detailed above we can make the following observations:

- ◆ There is an increase in milk production of between 10 to 12%.
- 10 ◆ Milk fat content increases between 18 to 20%.
- ◆ Protein content increases from 3 to 5%.
- ◆ There is a high concentration of vitamins and minerals in the milk.

As a result of less toxemia there is a higher degree of assimilation of nutrients of high biological value, better intestinal passage which results in a more vigorous feeding. Herds have
15 been observed to have a higher proportion of cows in heat as well as an increased response to successful artificial insemination.

Beef Cattle:

Certain observations have been made in beef cattle as a result of using this metabolic corrector, the most important being as follows:

- 20 ◆ More rapid weight gain and overall growth is observed in young weaning animals, when fed the metabolic corrector together with their milk.
- ◆ Cattle in pens have been observed to increase their weight between 30 to 40% more than the untreated norm.
- 25 ◆ Use of the metabolic corrector provides a higher carcass weight of the animals at slaughter.

Horses:

Sporting horses often live in an artificial environment (a box), with little or no light and are fed a ration which is brought by man. Generally horses under this medium live under a permanent state of stress. This medium often results in lack of appetite (anorexia); disturbances in the color and odor of the fecal matter; and exposure to colic. It is commonly observed, when exposed to a competitive environment, that these animals show a general lack of appetite and stress.

The use of the metabolic corrector in the ration results in a stabilization of the digestive process as shown in the normalization of the fecal matter, an increase in appetite shown under voluntary feeding and better performance under a training environment.

In addition, it has been observed that horses have improved their red blood cell formation (erythropoiesis), red blood cell count as well as an increase in the relative red blood cells in the plasma (hematocritical), which can be traced to the action of the metabolic corrector on the overall process of blood formation (hematopoiesis).

High Performance Laying Hens:

This is the sector where the metabolic corrector has been proven and tested the most, showing the following results:

- ◆ An increase of 5 to 6% in quantity of eggs laid
- ◆ A distinct difference in the distribution of egg size:
 - 15 to 35% more large size eggs
 - 20% less medium size eggs
 - 15 to 18% less small size eggs
- ◆ 2 to 4.5% increase in the weight of the egg
- ◆ Mortality due to viruses affecting the laying hen population was reduced by 50% on those hens being fed the corrector. It is felt that the utilization of the

metabolic corrector stimulates immune mechanisms, thus increasing the animal's natural defenses.

- ♦ Uniformity of weights (according to figures recommended by the developers of the genetic string of laying hens) is obtained more readily. The uniformity of weight on those treated hens was observed to be 20% higher than for the untreated hens.

The analytical content of Component A has been determined. It is made up of 15% water and 85% dry matter. The following details are based on the dry matter only:

10	A) <u>Metabolites:</u> (approximately)	
	- Proteins	34.80%
	- Fats	4.35%
	- Mineral Ashes	17.40%
	- Carbohydrates	39.10%
	- Fiber Content	4.35%
15	B) <u>Vitamins:</u> (in Milligrams per Kg. Dry Matter)	
	- Vitamin A (Beta Carotene)	40
	- Vitamin D (Calciferol)	5
	- Vitamin E (Tocopherol)	70
	- Vitamin B1 (Thiamine)	15
20	- Vitamin B12 (Riboflavin)	6
	- Vitamin C (Ascorbic Acid)	200
	- Panthotenic Acid	12
	- Niacin	50
	- Folic Acid	0.5
25	- Biotin	0.5

	C) <u>Amino Acids:</u> (in Milligrams/100 gr. Protein)	
	- Alanine	6
	- Arginine	5.5
	- Aspartic Acid	8.5
5	- Cysteine	0.5
	- Glutamic Acid	12
	- Glicine	3
	- Histidine	8.8
	- Tryptophane	0.9
10	- Tyrosine	1.8
	- Isoleucine	2.5
	- Leucine	3.5
	- Lysine	5.0
	- Methionine	1.0
15	- Phenilalanine	2.5
	- Proline	2.7
	- Serene	3.5
	- Treonine	2.8
	- Valline	3.0
20	- Cysteine	0.5
	- Citruline	2.0
	- Ornitine	1.5
	- Tyrosine	0.4
	- Treonine	0.3

	D)	<u>Mineral Content:</u> (in Milligrams/Kg. Dry Matter)	
		- Calcium	7,000
		- Sodium	11,000
		- Phosphorus	6,000
5		- Cobalt	3.5
		- Silver	0.5
		- Boron	70
		- Bromium	1
		- Chromium	1
10		- Copper	4
		- Iron	35
		- Iodine	450
		- Potassium	12,000
		- Magnesium	1,800
15		- Manganese	26
		- Molybdenum	0.1
		- Nickel	10
		- Sulfur	2,800
		- Strontium	1
20		- Vanadium	1
		- Zinc	35

The amounts of these components may vary. However, it is important that the algae, yeast, and calcite components of the metabolic corrector be used in their essentially intact form. For example, a synthetic combination of the analytically determined components of Component A does not achieve the results claimed heretofore. Likewise, the use of less than all three of the ingredients of the metabolic corrector may be beneficial but does not provide the optimal results according to the invention. Preferably, the algae, yeast, and calcite must all be present together to provide the surprising effectiveness of the metabolic corrector.

The genus *Macrocystis* is the largest algae in the family *Lessoniaceae*. It includes *M. pyrifera* L., *M. integrifolia* Bory, and *M. angustifolia* Bory. *M. pyrifera* is preferred, although

it is expected that other species may be employed pursuant to the invention. Algae of related genres include *Dictyoneurum*, *Pelagophycus*, and *Nereocystis*. The blades of the algae are the preferred components, although the entire plant may be used.

EXAMPLE 1

5 An experiment was conducted with cattle to determine whether the metabolic corrector provided a marked improvement in the general metabolism (specifically in the ruminal metabolism) of cattle through the use of human medical techniques, thereby improving the production of beef and milk. The specific objective of the experiment was to determine the correction of the digestive media through the use of diagnosed metabolic correctors in a milking
10 herd in Argentina. The breed of cattle was Holstein Fresian cows.

METHODOLOGY

Criteria in Selecting the Test Group.

The process of selection of the Test Group was based on the diagnosis of existing needs in the herd at a time where maximum milk production was required.

15 This period, between 0 to 90 days after calving, demands from the cow the use of all of its reserves to meet the highest nutritional requirements imperative at the time of maximum lactation.

By the same token, it is during this period that the cow must call on all its resources in order to replace tissue lost during parturition, thus preparing itself for the coming period of heat and pregnancy essential for the animal to be considered an economically productive unit.
20

As a first step, these were the criteria used in selecting the Test Group from the herd. No first pregnancy heifers were selected and were left for a later study of this same type. Thence two lots of ten (10) animals each were picked at random, each animal with an individual I.D. number. These two (2) groups are herein known as "Test Group" and "Control Group,"
25 respectively.

Initial Diagnosis

The diagnostic process began with the extraction of serum and blood samples from each individual animal. These samples provided a mineral content profile for each individual Group at the onset of the experience.

- 5 The minerals tested were those considered most lacking in the region. These minerals are: Calcium (Ca); Phosphorus (P); Magnesium (Mg); and Copper (Cu) as well as Total Protein and Albumin.

These profiles were analyzed taking into account the lab results and a diagnosis of the amounts lacking was effected.

10 Treatment

- A metabolic corrector was prescribed for the test herd in view of this diagnosis and taking into consideration the lactating period previously mentioned. The same formulation was used for all the cows in the test group. This metabolic corrector was fed twice a day at a rate of 100 grams/animal/day. The amount of metabolic corrector fed (100 grams/animal/day)
- 15 remained the same any time that the feed quantity was either changed or modified thus establishing a new relationship between the feed ration and the corrector.

Feed Management

- This experiment began on December 11th, 1992 with the analysis of each cow's milking record since October 15th, 1992, in order to determine the adjustments necessary as to
- 20 productions liters/day/cow as well as milk fat content. This was performed on each of the two Groups to avoid any misinterpretation of the final results.

Both Groups were handled jointly with the rest of the heard at milking time but were separated from the milking herd when they were put out to pasture. This insured that both test Groups were first to be on new pasture. This mode was used until December 30th, 1992 when

due to extreme drought conditions prevalent in the region since end November, required that the test Groups be handled together with the rest of the herd.

5 Pasture time on a daily rotating basis was set from 0800-1500 hrs - then milking; and from 1800-0400 hrs. - then milking. As of December 30th, 1992 the Groups were put into pens at night where good quality hay was provided after pasturing on grass.

Good quantity and volume of forage was provided both Groups during pasture; as the drought began to set in, this was changed to low volume-good quality forage during daytime and high volume-lower quality forage during the evening time when cows were in their pens.

10 During the milking, the cows were fed normal well balanced commercial feed (16% protein). The ration provided each animal depended on their milk production; both the "Test Group" as well as the "Control Group" were fed 5 Kg/cow/day (11 lbs./cow/day). This daily ration was divided in two, half being fed at each milking. The "Test Group" was fed the additional 100 grams per day of the prescribed metabolic corrector.

15 Normal sanitary conditions were kept during the whole experience; no cases of clinical mastitis were recorded in either Group.

The grazing sequence is shown in Table 1. The feed plants found in the Argentinean pastures are as follows:

20 Trebol Rojo - Red Clover (*trifolium pratensis*)
Pasto Ovillo - Sheep Grass (*dactylis glomerata*)
Sorgo Forrajero - Sorghum (*sorghum sacaratum*)
Agropiro (*agrophrum alongatum*)
Melilotus - Lotus (*mililotus officinalis*)
Moha de Hungria (*satarea italium pratensis*)
Phalaris (*phalaria bulbosa*)

TABLE "1" - Grazing (pasture) Sequence during the Experience.

Daytime Grazing		Nighttime Grazing	
Date	Type	Date	Type
Nov. 02 to Nov. 10, 1992	# 91 R. Clovr + Sheep Past	Nov. 2 to Nov. 8, 1992	# 90 Agropiro & Lotus
Nov. 11 to Nov. 19, 1992	# 90 R. Clovr + Sheep Past	Nov. 9 to Nov. 16, 1992	# 90 R. Clover Falaris.
Nov. 20 to Nov. 27, 1992	# 91 R. Clovr + Sheep Past	Nov. 17 to Nov. 29, 1992	# 89 Agropiro & Lotus
Nov. 28 to Dec. 2, 1992	# 90 R. Clovr + Sheep Past	Nov. 30 to Dec. 13, 1992	Bale of Moho 8.816 lbs./day/cow
Dec. 3 to Dec. 18 1992	# 89 R. Clovr + Sheep Past	Dec. 14 to Jan. 6, 1993	Bale of R. Clover 8.816 lbs./day/cow
Dec. 19 to Dec. 26, 1992	# 91 R. Clovr + Sheep Past		
Dec. 27 to Jan. 6, 1993	Sorghum Feed		

=====

Data Acquisition

The following Data Acquisition scheme was designed taking into account the specific objectives set forth at the onset:

- A) Individual milk production per cow in both Test as well as Control Groups.
 - 5 1) Initial Sampling
 - 2) Monthly Sampling
 - B) Milk Fat content (Grasa Albumina) in both Test as well as Control Groups.
 - 1) Initial Sampling
 - 2) Monthly Sampling
- 10 The Initial Milk Production Sample (under A-1) was obtained from the Control Sheets kept by *CASTELMAR*, the local dairy farmer's coop.
- Subsequent Monthly Samples (under A-2) were taken in the same manner for the months of November, December (1992) and January 1993.
- 15 Table "2" provides a comparison of Milk Production in the "Test Group," the "Control Group" as well as the whole of the milking herd. A graph is provided as Fig. 1.

TABLE "2" - Milk Production Records - Test Group & Control Group - compared

Cow I.D. No.	Calving Date	No. of Calves	Lactat. Days	MILK PRODUCTION CONTROL			
				Oct. 14	Nov. 16	Dec. 12	Jan. 15
"CONTROL GROUP"							
508	9/01/92	7	43	33.4	24.0	20.6	20.0
755	8/23/92	3	52	34.6	29.6	16.6	20.0
862	8/09/92	2	66	25.4	25.2	14.8	19.4
878	7/26/92	2	80	23.8	26.0	13.8	13.8
893	9/01/92	2	43	27.4	25.8	14.6	18.6
896	9/25/92	2	19	24.7	26.4	20.2	19.8
979	9/23/92	3	21	28.4	19.8	16.2	18.2
1129	9/05/92	5	39	22.0	19.6	16.4	14.4
1131	8/01/92	3	74	28.4	21.2	14.2	16.4
1145	7/30/92	3	76	30.2	20.0	14.8	20.0
Ave. Milk Production			52	27.8	23.7	16.2	18.0
"TEST GROUP"							
541	9/02/92	7	35	33.8	30.0	21.0	23.2
694	8/16/92	3	59	33.8	28.4	19.0	26.0
738	9/15/92	3	28	33.0	27.4	17.2	21.2
764	8/15/92	3	60	27.6	23.4	17.2	18.4
818	9/05/92	2	39	34.6	30.0	20.4	22.2
964	8/16/92	2	59	27.3	24.6	17.0	21.6
989	9/25/92	2	19	26.8	27.0	20.8	20.4
1000	9/22/92	5	22	26.6	22.4	17.4	19.8
1093	7/20/92	5	86	31.6	27.4	16.4	17.8
1141	7/21/92	3	85	26.6	24.2	17.2	18.4
Ave. Milk Production			52	29.8	26.6	18.5	21.0
DIFFERENCES FOUND IN %:				+7.2%	+12.2%	+13.6%	+16.6%

At the onset of the Experiment the Lactation Period for the "Control Group" was 52 days and 50 days for the "Test Group". These periods have been adjusted for variances using tables provided by the S.R.A. - Sociedad Rural Argentina - which take into consideration adjustment of lactation periods of 305 days as related to age. Table "3" contains the relevant information from these tables.

TABLE "3" - Lactation Periods to 305 days - Conversion Table used

	No. OF LACT. DAYS	AGE AT PARTUM (in yrs. & decimals)		No. OF LACT. DAYS	AGE AT PARTUM (in yrs. & decimals)	
		<3 years	>3 years		<3 years	>3 years
10	15	16.67	14.63	165	1.62	1.51
	35	9.99	8.9	175	1.54	1.44
	35	7.13	6.36	185	1.47	1.38
	45	5.54	4.96	195	1.41	1.33
	55	4.53	4.07	205	1.35	1.28
15	65	3.85	3.48	215	1.3	1.24
	75	3.35	3.02	225	1.25	1.2
	85	2.97	2.69	235	1.21	1.16
	95	2.68	2.43	245	1.17	1.14
	105	2.44	2.22	255	1.13	1.1
20	115	2.25	2.05	265	1.1	1.07
	125	2.08	1.91	275	1.07	1.05
	135	1.94	1.79	285	1.05	1.03
	145	1.82	1.68	295	1.02	1.02
	155	1.72	1.59	305	1	1
25						

Conversion Factors - To Equivalent Age

(in months)

5

10

15

20

25

Age at Last Partum	FACTOR	Age at Last Partum	FACTOR
21	1.44	72	1.01
24	1.35	78	1
30	1.31	84	1
32	1.26	90	1
33	1.21	96	1
36	1.15	102	1
42	1.1	108	1.02
48	1.06	114	1.02
54	1	120	1.03
60	1.04		

30

Cows were not given their feed rations from Dec. 9 through Dec. 12, 1992. Coincidental with this lack of feed, the month of December shows a marked decline in milk production during this period. Regardless of this fact, the Milk Production Control for this month was kept as scheduled. It was felt that, in order not to affect the results of the experiment, the recordings were to be kept as initially programmed.

Table "4" provides a comparison in Milk Fat Content for the "Test Group," the "Control Group" as well as the whole of the milking herd. A graph depicting these quantities is also provided as Fig. 2.

TABLE "4" - Milk Fat Content - Test Group & Control Group - compared.

		(Grass/Fat)							
		October		November		December		January	
LOT		14/92		16/92		12/92 15/92			
		Gr.	% Fat	Gr.	% Fat	Gr.	% Fat	Gr.	% Fat
Control Group		867	3.11	831	3.50	515	3.17	559	3.10
Test Group		1009	3.39	875	3.29	622	3.38	688	3.27
		+142		+44		+107		+129	
DIFFERENCE		+16.4%		+5.8%		+20.8%		+23.2%	
Total Milk Pool				595		507		500	

Several conclusions can be drawn from this Example. First, the palatability of the metabolic corrector added to the ration was acceptable to the "Test Group." Second, judging from the results obtained from this Experiment the differences between the "Test Group" and the "Control Group" both in milk production as well as in fat content gradually increased with time. Thus, one can conclude that, in time, the metabolic corrector has a cumulative beneficial effect in the animal's rumen. Third, there was a definite residual effect on the "Test Group." Independent sources recorded this effect as far as February 5th, 1993 before the rest of the herd was fed the metabolic corrector.

Finally, from the results of this Experiment one can definitely conclude that the metabolic corrector does have utility and economic potential in larger dairy herds.

EXAMPLE 2

5 An experiment was conducted with beef cattle to determine the effect of the metabolic corrector on weight increase. A test group consisting of 70 head of steers was divided out of a herd, of which 353 head remained as the control group. All animals were fed on a winter pasture of barley grass and rye grass, at a load of about 400 kg/hectare, or about 616 lbs/acre. The test group was fed with fresh forage plus 2.2 lbs of corn per day, and 20 grams of the metabolic corrector, as with the dairy cattle. The control animals had the same diet, but without the metabolic corrector.

10 The test animals were slightly lighter, on average, than the control group, but they were otherwise comparable. The average weights of the animals at the beginning of the experiment is shown in Table 5.

The experiment began September 14 and ended December 7, 1993, 84 days later. The final comparative analysis in Table 5 shows that the average daily increase and total increase in weight for the test group, in terms of percentage, was more than double the increases for the control group. The total increase averaged 142 lbs, or about 60% for the test animals, as compared to 93.8 lbs, or 28% for the control animals.

This experiment demonstrates that the metabolic corrector can increase the rate of weight gain for beef cattle, at least over the course of several months.

Table 5
Results of the Beef Experience

*****					TEST GROUP			CONTROL		
GROUP										
Date	Day	Wt(Lb)	Gain	%	Wt(Lb)	Gain	%			
9/14	0	236.5	-0	-0	335.2	-0	-0			
10/08	24	275.5	39	16.5	360.8	25.8	7.7			
11/06	29	329.8	54.25	19.7	390	29.36	8.13			
12/07	31	378.5	48.7	14.77	429	38.68	9.91			

Final Comparative Analysis

	Test Group	Control Group
Daily Increase	1.69 Lbs.	1.117 Lbs.
% Increase	0.7 %	0.3 %
Total Increase	142 Lbs.	93.8 Lbs.
% Increase	60.04 %	28 %

Modifications and variations of the above-described embodiments of the present invention are possible, as appreciated by those skilled in the art in light of the above teachings. It is therefore to be understood that, within the scope of the appended claims and their equivalents, the invention may be practiced otherwise than as specifically described.

The invention uses natural elements in essentially intact form (high concentration kelp, dried and crushed; live yeast in microcapsules; supplemented by calcite). The specification does not call for subjecting these components to heat, which would kill the yeast and alter the intact form of the algae. The metabolic corrector works as a nutritional "buffer" and allows for adequate absorption of the metabolites in the feed ration.

Unlike most nutritional supplements, which are dried after having been subjected to intense heat, the constituents of the metabolic corrector are provided in their natural form, essentially intact, not as a consequence of exposure to high temperatures.

The metabolic corrector is comprised of certain substances that once introduced in the digestive system, are highly synergistic on the components thereof, the results of which are reflected in the animal's optimized health, a better assimilation of nutrients, higher production efficiency and natural augmentation of the immune system action of each species.

The metabolic corrector is not a mere nutrient source. It is not a feed in itself but is added to animal feeds. It is comprised of natural substances which, in essentially intact form and in certain quantities, help in the metabolic processes of animals, allowing regulation of digestion physiology, such as pH levels in ruminants. Within the organism, at bodily temperature, the metabolic corrector achieves remarkable increases in the animal's productive response, presumably due to improved absorption of essential nutrients, stabilizing changes in elements, micro elements and metabolites in general.

When trace elements in animal feeds are taken via the intestinal mucous membrane and absorbed into the blood stream, they join with carrier proteins (apoenzymes) which provide the cells with the metals and nutrients required for metabolism, and may be stored in the liver. The use of heat in the food industry (animal and human) can destroy the apoenzyme bonds rich in trace elements present in grain. For example, the nutritional value of Cobalt (Co), Copper (Cu), Manganese (Mn), Zinc (Zn), Chromium (Cr), Selenium (Se) can be lost.

For example, with high genetic quality laying hens, field tests showed that no undigested remnants were found in the feces, whether looked under the

microscope or not, showing a greater utilization of grains in the diet. This information allows treatment of the serious economic problem of the weak absorption syndrome (Buxade-Carbo, Spain). Thus, the metabolic corrector acts as a diet balancer providing nutrient requirements at the precise location and moment of the delicate digestive process.

High temperatures and chemical processes are not used to dry or preserve any element. The animal's bodily temperature develops the specific actions of the inventive composition.

The composition of the invention is not a mere nutrient source or feed but a metabolic corrector that is added to animal feeds. It helps in the metabolic processes of animals, allowing regulation of digestion physiology. Within the organism, at bodily temperature, it achieves enhance absorption of essential nutrients, stabilizes changes in elements, microelements and metabolites in general, and is therefore highly beneficial for the animal by holistic criteria. It also allows remarkable increases in the animal's productivity (eupeptic action). The product can regulate pH levels like a buffer).

A preferred embodiment comprises:

(A) Algae dried at low temperatures (air or open air, at low temperatures) and mechanically ground (e.g. by hammer mill).

(B) Living, dry yeast Cultures, encapsulated in "tiny pearls" by the manufacturer, for example those identified as *Cepa Sc Saccharomyces cerevisiae*.

C) Calcite, containing macro and micro minerals according to the established requirements for each species.

The invention employs holistic principles of medicine (the whole animal system is analyzed and not a specific organ). The gastrointestinal medium serves as fermentation vessel where nutrients are naturally supplied and released and where microorganisms are freely reproduced (living yeasts). There is a synergistic enhancement and interaction reflected in the animal's optimized health, a better assimilation of nutrients, more production efficiency and natural augmentation of the immune system action of each species.

The kelp is believed to serve as a substrate or "culture

medium" within the animal itself, so that living, high concentration yeast may fully develop its fermentation power. Once introduced in the digestive system, the dried kelp hydrates and due to moisture and bodily temperature and the agar nature thereof, forms a viscous gel, a colloidal suspension of mucopolysaccharides, so that the composition may slowly release natural components (vitamins, proteins, carbohydrates, aminoacids, minerals and trace elements or coenzymes). The kelp is believed to act as a chelating agent (a phycocolloid), improving bioavailability of e.g. minerals, trace elements, carbohydrates, vitamins, and coenzymes.

Algae have a large content of polyunsaturated fats, i.e. palmitic, stearic, miristic, agraquidonic, linolenic, gamma-linolenic (Henrikson). These essential fatty acids (EFA) have multiple actions e.g.: they help normalize cholesterol levels; they are forerunners of prostaglanclins; and they retard premature aging processes.

High concentration, living yeast is used (probiotic). The AAFCO (Association of American Feed Control Offices) of the U.S.A. defines "living yeast cultures" as a dry product of living yeast and medium retaining fermentation power. Microencapsulated yeast has important benefits: the yeast reaches the digestive system intact. The yeast used according to the invention is dry but it is preferably live, active, latent yeast and it keeps its power to ferment unlike feed or brewer's yeasts that are inactive. One commercially available example comprises yeast cultivated in a substrate of sugar cane syrup which is used to encapsulate the living yeast. The active substance is comprised of viable cells of *Saccharomyces cerevisiae*, SC 47 Strain. This example is High Concentration Yeast, Biosaf SC 47 available from Societe Industrielle Lessaffre, Marcq-En-Baroeul-France. This type of living, high concentration yeast contains 5×10^9 living cells per gram. Other types of living, high concentration yeast may be used if they have the necessary latency from microencapsulation and fermentation power. The process to dry living high concentration yeasts is carried out at temperatures not higher than about 50° C, preferably below about 30° C.

The use of such yeast in fermentation in the animal with the culture medium of algae as support causes stimulation and supply of nutrients to the

normal microflora and the conversion of non proteinic nitrogen, specifically ammonia, NH_3 , into bacterial proteins of high biological value.

5 Calcite is beneficial both because it provides its own components and is a micronutrient excipient. An excipient is an inert substance used for combining with a drug for desired bulk, taste, or other characteristics to simplify its use.

10 Modern man subjects animals to the "stress" of captivity to obtain better productivity. This means that captive animals cannot choose freely their feed, which is chosen by man according to the components of each ingredient and the price. The price of inputs determines, to a great extent, the composition of balanced feeds, what do not always agree with the animals' requirements. Furthermore, cereal and grain treatment techniques with chemicals (herbicides, pesticides, agrochemicals in general) and later crops treated with physical drying processes (heat), render grains less desirable than those that are naturally dried. In other words, the components of "balanced feeds" reach manufacturing stages already denatured by physical and chemical agents. Moreover, the balancing process further damages grains due to the use of heat. In addition, recent investigations show that the use of agrochemicals produce metabolic changes in plant crops, altering or hindering nutrient (minerals present in the soil) absorption mechanisms.

20 Standard methods of detecting nutritional deficiencies rely on blood mineral profiles. However, a bloodprofile is only an instantaneous photograph; the values obtained depend on the intake composition at that precise moment and may vary if time elapses from such intake. For example: blood composition is not the same if tested during fast or after a big meal. Metabolite levels in both samples vary. Accordingly, a test was needed that allows analysis of the "mineral history" of the animal.

30 The mineralogram according to the invention may be a hair, feather, hoof, or nail test. This makes it possible to detect the effect of factors external to the organism (toxic minerals, nourishment, climate, captivity, etc.) which may influence future productivity.

Mineralogram diagnosis is supported by works made by the French School of Functional Medicine, which uses the following diagnosis methods:

a) mass spectrometry

- b) molecular mass chromatography
- c) magnetic resonance spectroscopy

These tests find trace minerals present in hair, feathers, and fur proteins and accurately detect excess as well as lacks of micro and macro minerals.

Trace elements, vitamins and aminoacids are bound or linked in complex interactions. (Pauling, Embid, Ortega, Dorrignol). Sea calcite may be used to contain and transport micro and macro minerals included in the formulation for each species.

The invention uses the digestive system as a path and the animal feed as a carrier to introduce the product into the gastrointestinal system, where natural seaweeds act as a culture medium and nutrient supply, causing the gel or colloid formed with the digestive system fluids (moisture) at bodily temperature to develop and living yeast to multiply. Simultaneously, a series of important interactions, reactions and metabolite release begins to take place in the digestive system. The algae form a viscous gel when the product contacts gastric juices; this enhances reproduction of living yeast, slowly releasing the components thereof, in conjunction with calcite, which helps regulate pH levels and delivers micronutrients. Industrial processing is not needed to cause the desired effects.

The product has eupeptic action, as a drug that improves food digestion and increases hunger, and a eutrophic action, as it induces the animal to build biomass with abundant nutrients.

MANUFACTURING

The three basic components, in the quantity desired, are placed in a regular mixer (as typically usually used in feed factories). The preparation should be mixed for about 30 minutes to attain a homogenous mixture, and then is turned into powder pellets. Once the mixing process is completed, the product is packed in containers such as cardboard, two-ply paper sacks, or polypropylene. Preferably, the part of the container which contacts the product should be water-resistant for better preservation, since the final product is hygroscopic ("absorbing or attracting moisture from the air according to environmental conditions"). Once the product is packed, it should be stored in dry, closed places, at ambient temperature below about 50°

C. The finished and presented product is ready to be added to animal feeds per use and quantity instructions.

5 Different flavorings can be added to the product to obtain better acceptance by the animal under treatment (for example: honey or apple flavorings for swine and garlic flavorings for dogs). As flavorings are used in small quantities, same should be previously "stretched" with one of the components of the product (for example, calcite).

INTERACTION OF THE COMPONENTS OF THE METABOLIC CORRECTOR

Phase I:

10 The composition as part of the daily ration is subjected to mastication (chewing) and the action of the salivary gland secretions and thus is attacked by the salivary enzymes (amylases) and the physical action of the mastication process.

Phase II:

15 In monogastric animals, the metabolic corrector is ingested and, after the inherent process of chewing and primary enzymatic action, it is then subjected to further bacterial and protozoogenic action (with pepsins and stomach hydrochloric acids coming in to play) and thus the biodegradation of the ingested foods begins to take effect.

20 Polygastric animals (ruminants) further subject the ingested feed to normal digestive floral action as well as the mechanical (pressing) action typical of the polygastric stomach. Regurgitation occurs as part of the normal ruminant process with consequent ingestion into the obomassums where the feed bolus is further subjected to the action of the digestive juices.

25 In these processes the composition is subjected to both bacterial and enzymatic action.

30 Upon being ingested, the corrector is subjected to hydration at rumen temperature (37° C). The live yeast emerge from their latent state and begin to perform those (eupeptic) actions contributing to improved digestion and metabolic absorption of all available nutrients. This occurs basically through the utilization of non-proteinic nitrogen. These ruminal processes end with the creation of volatile fatty and aminoacids i.e., acetic, butyric and

propionic. By the same token, the NH₃ is transformed into bacterial proteins of high biological value in the improvement of the animal's productivity. The metabolic corrector also helps with breakdown of fiber.

Phase III:

5 Following the gastro-ruminal phase is the gastro-intestinal phase where pancreatic amylases, proteases and lipases, together with the detergent action of the liver bile subject the feed components as well as the corrector to further degradation. This is the end of the physical-chemical degradation process.

10 Normal intestinal flora develops its own fermentation process. After routine use of the metabolic corrector has been established (15 to 20 days) this intestinal flora is believed to begin to attach itself to the cellular walls of the algae.

15 Edible algae used in the formulation of the invention live and reproduce in a marine environment and thus develop walls which are made of cellulose and lignin. The surrounding environment where these algae prosper is of a lower temperature. This, together with the action of the sea and the rocks, call for a natural survival reaction from the algae resulting in the strengthening of these cellular walls. Normal intestinal flora develop which attach themselves
20 to these walls by cellulolytic action. This takes place during the period of 15 to 20 days mentioned above.

25 Then, the feed and the metabolic corrector combined with body heat and ruminal humidity, and subjected to the processes described above, with the help of the agar, forms a colloidal suspension which attaches itself to the intestinal epithelial walls. It is here, in the intimate reaches of the capillary celiac, where the metabolic corrector is believed to release the carbohydrates, proteic amino acids, lipids, micro and macro minerals and
30 vitamins to the circulatory system of the animal.

DOSAGE

30 Medical technology and veterinary practice correlate dosage of elements to the weight of the individual. To obtain the recommended dosages a trial and error method can be used. Original dosages were based on clinical studies and results from mineral analysis of the individual or individuals. Beginning dosages were calculated to provide a metabolic correction. There were no

negative adverse reactions to mega-doses, except perhaps a small laxative effect.

Restated, the metabolic corrector is used as a supplement for animal feeds, and is comprised of cold-dried *Macrosystis Pyrifera* algae, living high concentration yeast in the form of microcapsules and dried in the capsular medium, and calcite with mineral components pursuant to the requirements of each species. The metabolic corrector is used in a process developed within the digestive system of the animal at bodily temperature with the algae as culture medium; this interacts with and allows development of living, high concentration yeasts which, with calcite supplement, improves the development and use of minerals, carbohydrates, vitamins and trace elements.

The process of the invention uses the culture medium of the animal's digestive system, at bodily temperature, developed with *Macrosystis* algae, wherein living yeast cells reproduce "in situ". Metabolite measurement results are needed to prepare the combination required by each species. The method of the invention improves the animal's health through enhanced nutrient release as a consequence of the interaction of *Macrosystis* algae, living, high concentration, encapsulated yeasts, and calcite.

Practical experience with the metabolic corrector showed the following results:

1. In a test of laying hens, egg production was markedly increased as well as egg size and regularity.

2. In a herd of milking cows, coelum was effectively regulated which resulted in the proper and most economical use of artificial insemination.

WHAT IS CLAIMED IS:

1. A metabolic corrector for animals comprising *Macrocystis* algae meal, dry live yeast, and a mineral component, all in essentially intact form, the metabolic corrector forming a viscous, gelatinous preparation when combined with warm water.

2. The metabolic corrector of claim 1 in which the mineral component is powdered calcite from sea shells.

3. The metabolic corrector of claim 2 in which the algae is dried and crushed to a meal, and the yeast is *Saccharomyces cerevisiae* in microcapsules.

4. The metabolic corrector of claim 1 in which the algae is dried and crushed to a meal, the yeast is *Saccharomyces cerevisiae* in microcapsules, and the mineral component is powdered calcite.

5. The metabolic corrector of claim 2 in which the *Macrocystis* algae comprises about 25% to about 75% by weight, the yeast comprises about 10% to about 50% by weight, and the powdered calcite comprises about 10% to about 30% by weight.

6. The metabolic corrector of claim 4 in which the *Macrocystis* algae comprises about 50% by weight, the yeast comprises about 30% by weight, and the powdered calcite comprises about 20% by weight.

7. A metabolic corrector for animals comprising about 25% to about 75% of an algae of the family *Lessoniaceae*, dried and crushed, about 10% to about 50% dry live yeast, and about 10% to about 30% powdered calcite all in essentially intact form, the metabolic corrector forming a viscous gelatinous preparation when mixed with warm water.

8. A method of improving the health of an animal comprising:

- (a) measuring metabolite levels in a stable tissue of the animal;
- (b) identifying metabolites whose levels are lower than desired;
- (c) adding the identified metabolites to crushed calcite;
- (d) combining the calcite with essentially intact *Macrocystis* algae

meal and live yeast to provide a metabolic corrector;

(e) feeding the metabolic corrector to the animal, the components of the metabolic corrector interacting to provide health benefits to the animal.

9. The method of claim 8 in which the calcite comprises about 10% to about 30%, the algae comprises about 25% to about 75%, and the yeast comprises

about 10% to about 50%.

10. The method of claim 8 in which the metabolic corrector is provided in an amount of about 0.1g to 1.0 g per kg body weight.

5 11. A method of improving the health of an animal comprising combining crushed calcite with essentially intact *Macrocytis* algae meal and live yeast to provide a metabolic corrector, and feeding the metabolic corrector to the animal in an amount sufficient to provide health benefits to the animal.

12. The metabolic corrector of claim 7 in which the yeast is in microcapsules.

10 13. The metabolic corrector of claim 12 in which the yeast is *Saccharomyces cereviseae*.

14. The method of claim 11, in which the animal is a dairy cow and feeding the metabolic corrector to the cow for several months improves milk production and fat content.

15 15. The method of claim 11, in which the animal is a ruminant and the metabolic corrector adjusts the pH of the ruminal medium to a desirable level and improves digestive metabolism.

16. The method of claim 11, in which the metabolic corrector is fed to beef cattle for several months, and increases the rate of weight gain.

20 17. The method of claim 11, in which the animal is a horse and the metabolic corrector stabilizes the digestive process, normalizes fecal matter, and increases appetite.

25 18. The method of claim 11, in which the animal is a hen and feeding the metabolic corrector increases the quantity and size of eggs laid, and reduces viral mortality.

1/2

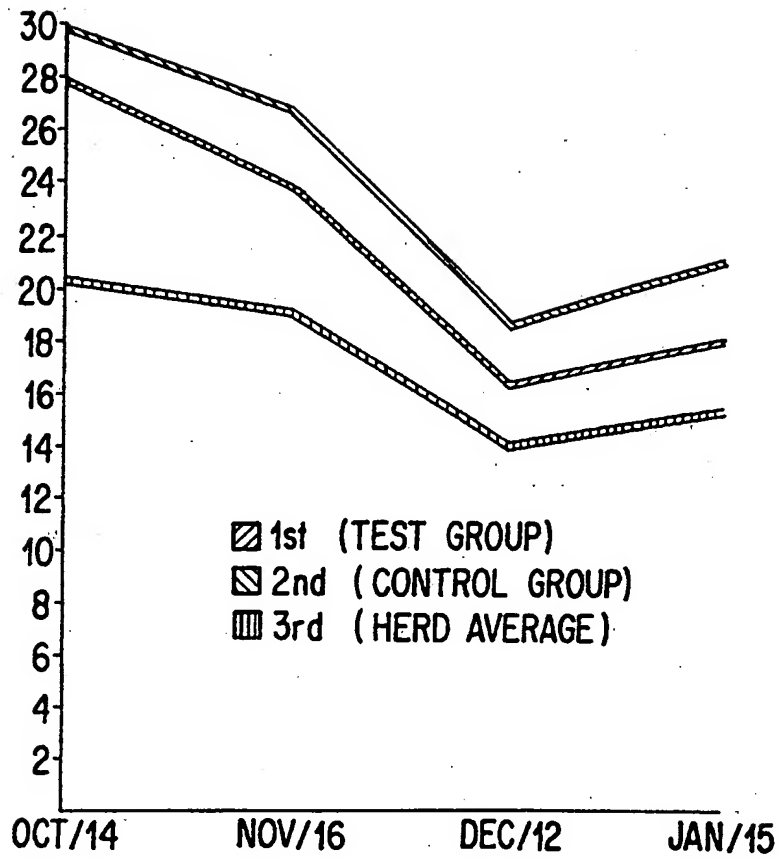


FIG. 1

2/2

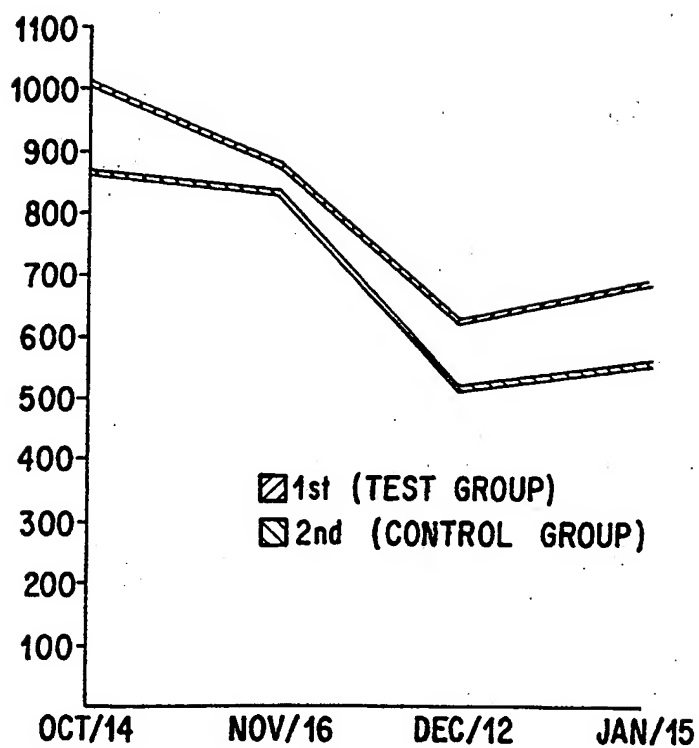


FIG. 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/08470

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A23K 1/00, 1/06, 1/175

US CL :426/002, 61, 74

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 426/002, 61, 74

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, DIALOG

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,087,556 (HARTE) 02 May 1978, col.4, lines 32-49; col. 8, claims 1 and 12.	1-13
Y	US, A, 3,876,810 (CARBONNIERE) 08 April 1975, col. 1, lines 12-22.	1-13
Y	Introduction to the Algae: Structure and Reproduction, Second Edition, issued 1985, H. C. Bold and M. J. Wynne, "Division Phaeophyta", pages 365 - 374.	7
Y	Gonzalez, C., BIOSIS PREVIEWS: 93060361, Cuban Journal of Agricultural Science, (1991) 25(1) 77-81, abstract	1-13
Y	NADAADIN, M., 91-035645 AGRIS International, Veterinarski glasnik, (1988) 42(9) 591-598, abstract.	1-13

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z	document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means		
P document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

25 SEPTEMBER 1995

Date of mailing of the international search report

03 NOV 1995

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/08470

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HUSKIC, L., 921446661 CAB ABSTRACTS, Praxis Veterinaria (Zagreb), (1990) 38(2) 123-130, abstract.	1-13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/08470

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-13

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/08470

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

1. Improving milk production and fat content in a dairy cow
2. Adjusting the pH of the ruminal medium and improving digestive metabolism in a ruminant
3. Increasing the rate of weight gain in beef cattle
4. Stabilizing the digestive process in a horse
5. Increasing appetite in a horse
6. Increasing the quality and size of eggs laid by a hen
7. Reducing viral mortality of a hen

The claims are deemed to correspond to the species listed above in the following manner:

Species 1-3 correspond to claims 14-16; species 4 & 5 correspond to claim 17; species 6 & 7 correspond to claim 18

The following claim is generic: claim 11

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the species affects the health of different animals in different ways and one method is not obvious over the other. In addition, each species would require a search on specific metabolic effects, even though the same composition is used for all the species.